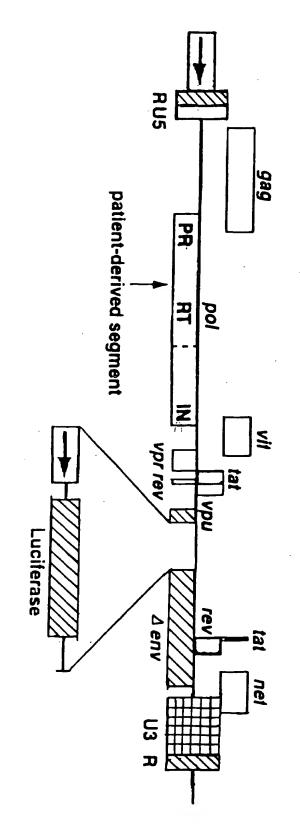
1

FIG. 1

# PhenoSense<sup>TM</sup> HIV Resistance Test Vector.



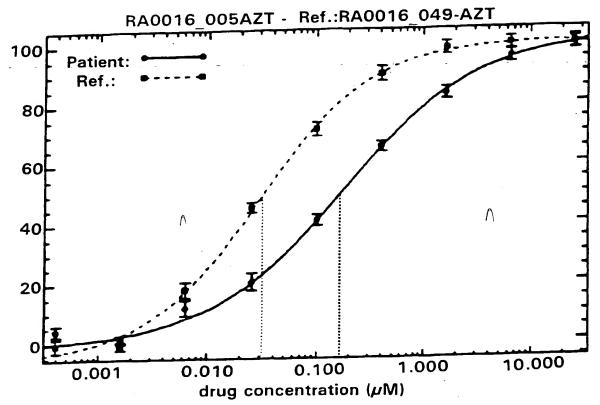
### FIG. 2

## PhenoSense™ HIV Schematic Diagram.

Resistance Test Vector DNA Amphotropic MLV env DNA Transfection PRI Λ Infection Luciferas Assay



### NRTI - AZT



AZT-Control

 $IC_{50} = 0.032$ 

**AZT-Patient** 

 $IC_{50} = 0.170 (5.2\text{-fold})$ 

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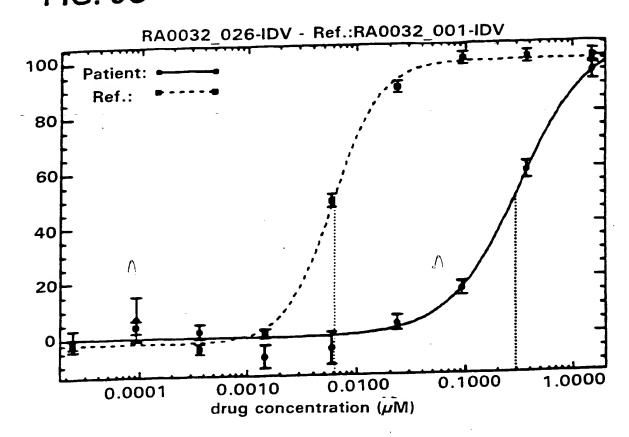
NNRTI - Efavirenz FIG. 3B MA0010\_011-EFV - Ref.:MA0010\_019-EFV 100 Patient: Ref.: 80 60 40  $\Lambda$ 20 1.0E-2 1.0E-1 1.0E-3 1.0E-4 1.0E-5 drug concentration ( $\mu$ M)

**EFV-Control** 

 $IC_{50} = 0.0015$ 

 $IC_{50} = 0.0380 (25.6\text{-fold})$ **EFV-Patient** 

FIG. 3C PRI - Indinavir



IDV-Control

 $IC_{50} = 0.0062$ 

IDV-Patient

 $IC_{50} = 0.2935 (47.4-fold)$ 



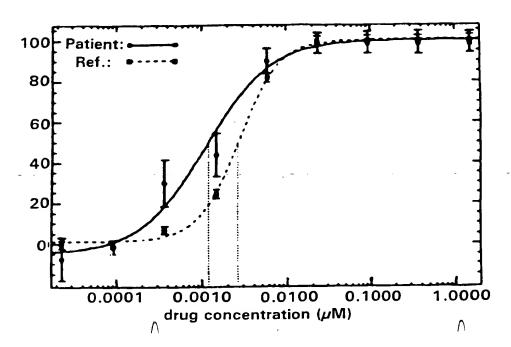
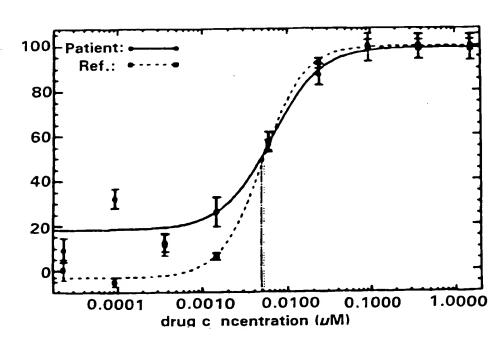


FIG. 4B IDV





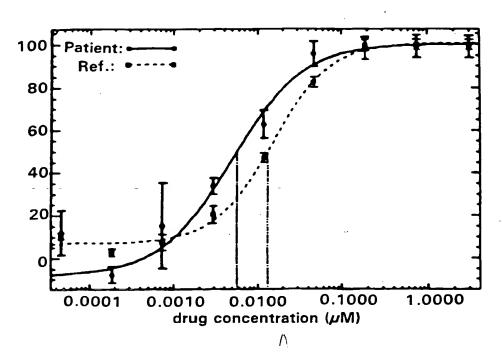
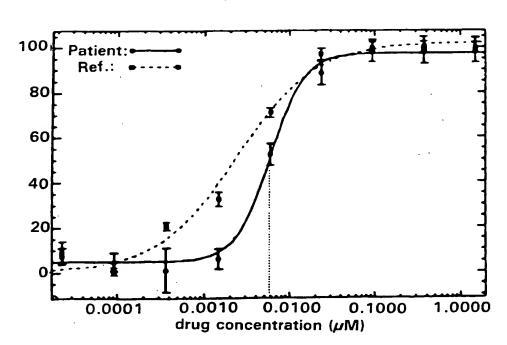
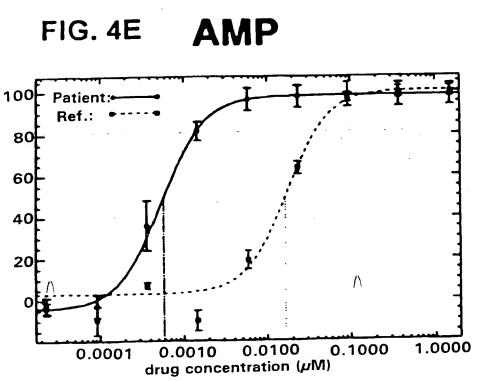


FIG. 4D NFV



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FIG. 5A SQV

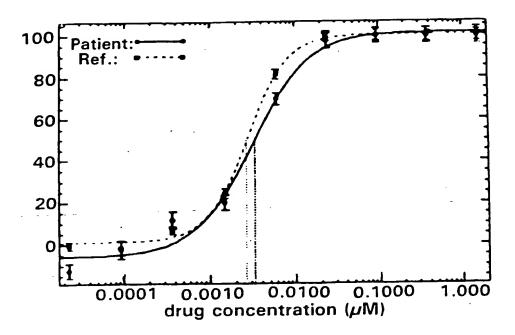


FIG. 5B IDV

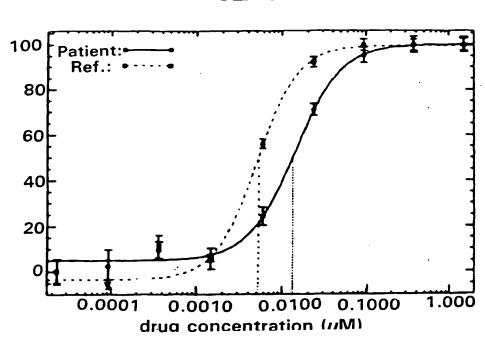
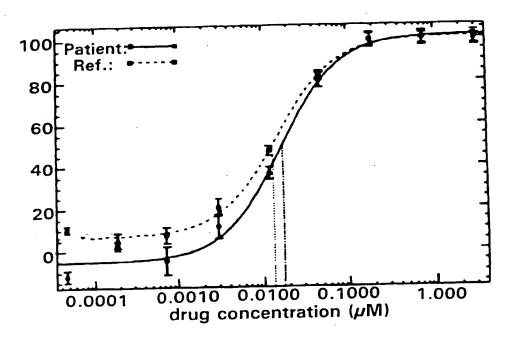
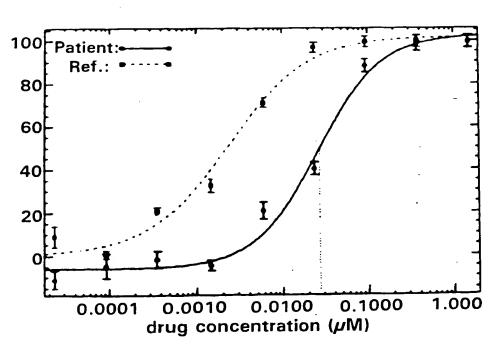
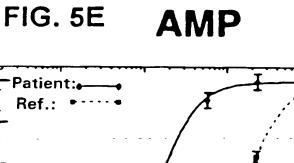


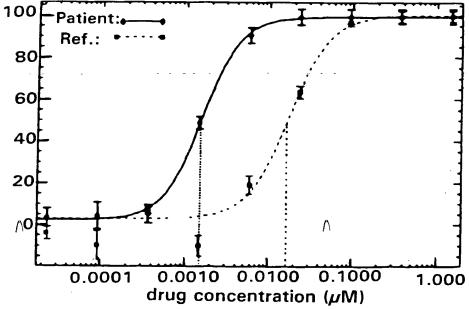
FIG. 5C RTV











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### Figure A: Fitness Assav

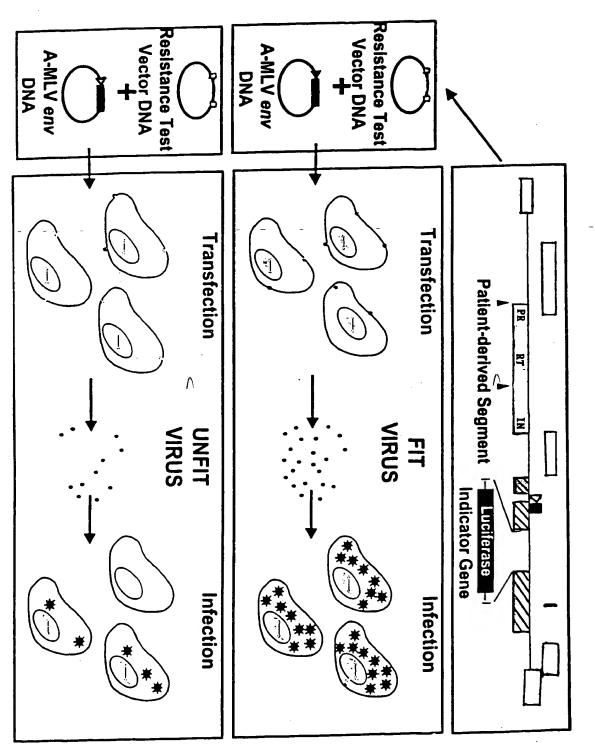
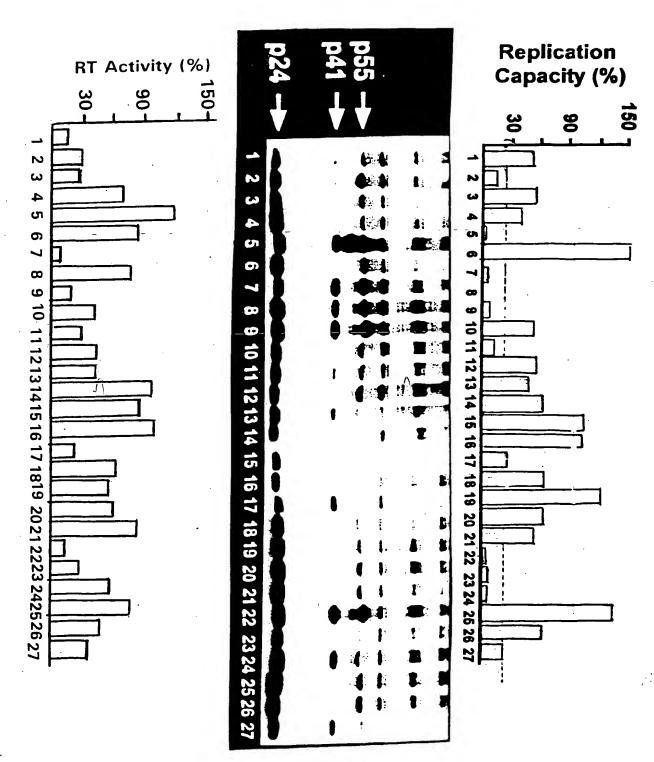


Figure B: Luciferase Activity in Infected Cells

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Luciferase Activity (x10 <sup>5</sup> RLU)										
		<b>Ω</b> 1	C	-	<u> </u>		<b>N</b>	,	.s	4
	<b>=</b>	20								
	Time After Infection (h)	0 35								
		5 50								
	Infe						Y	٦		
	ction	65 8	*					<i>\</i>	•	
	<u>(T</u>	90 9								
		95	-	4		<u>↑</u>	4	• •		
			·P3	P2	}	P T	Ker			
			PRI			NNRTI		NRTI		
	AMP	NFV	RTV	١D٧	SQV	ł	3ТС	AZT		Fold R
	4	57	1	30	17	40	>100	27	P 1	Fold Resistance
	18	55	62	47	83	0.3	ယ	17	P 2	nce
	ယ	28	63	39	4	0.3	>100	6	P 3	

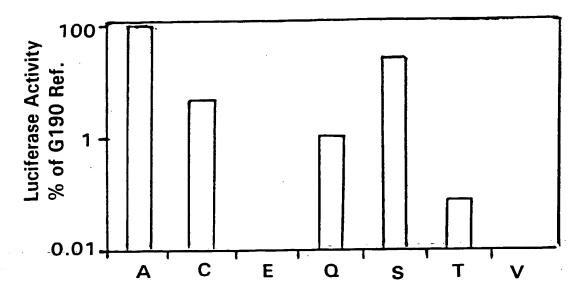
Λ :

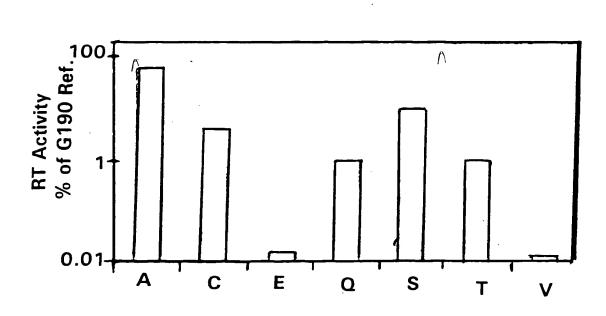


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Figure C: R plication Fitness, PR Processing, and RT Activity

Figure D: Site Directed RT Mutants (G190 Series)





G190 Mutants

$$A = Ala$$
  $C = Cys$   
 $E = Glu$   $Q = Gln$   
 $S = S$   $r$   $T = Thr$ 

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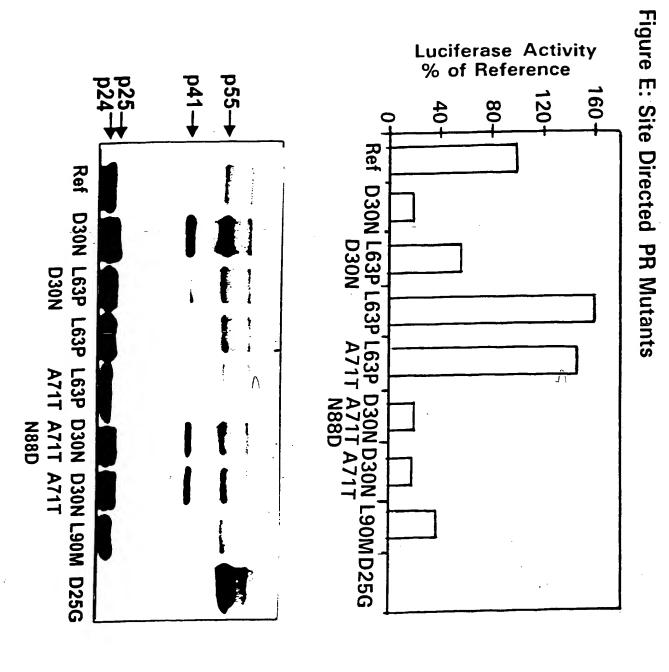
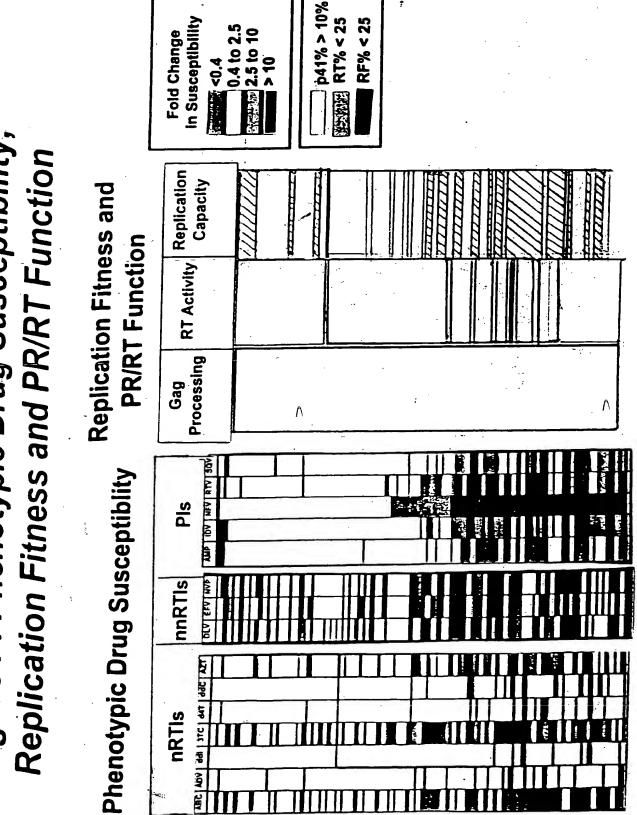
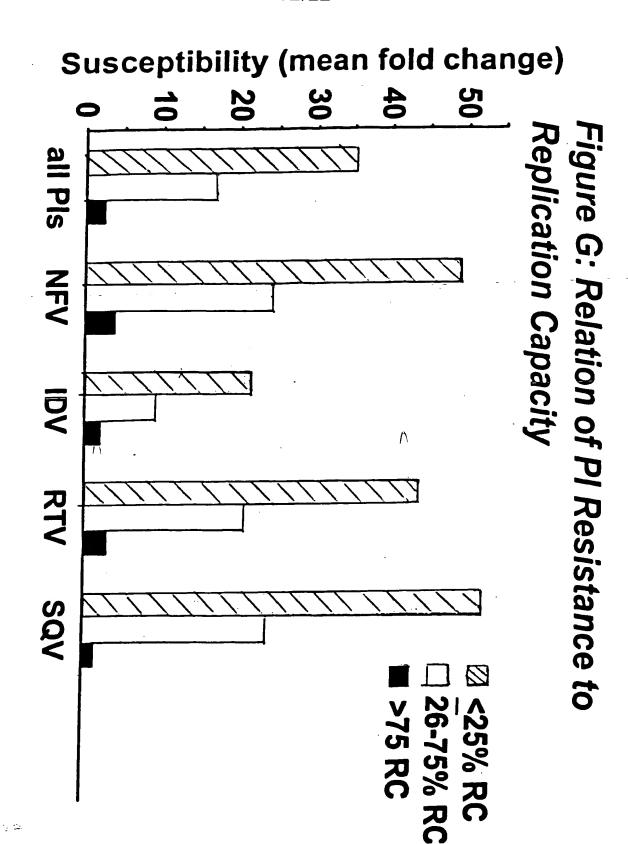


Figure F: Phenotypic Drug Susceptibility,





### Susceptibility (mean fold change)

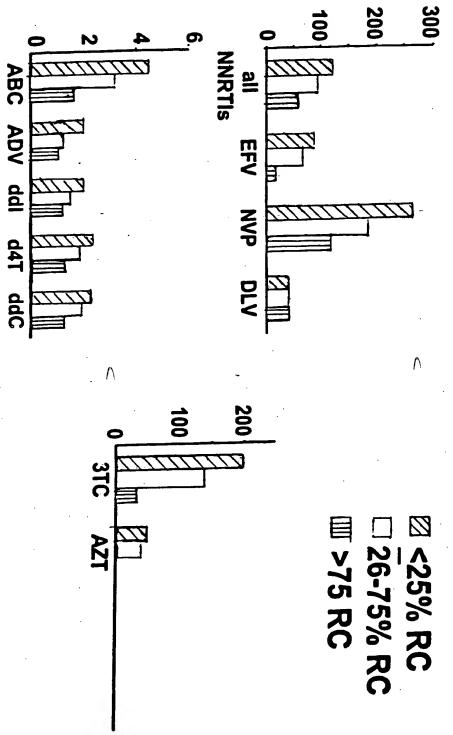
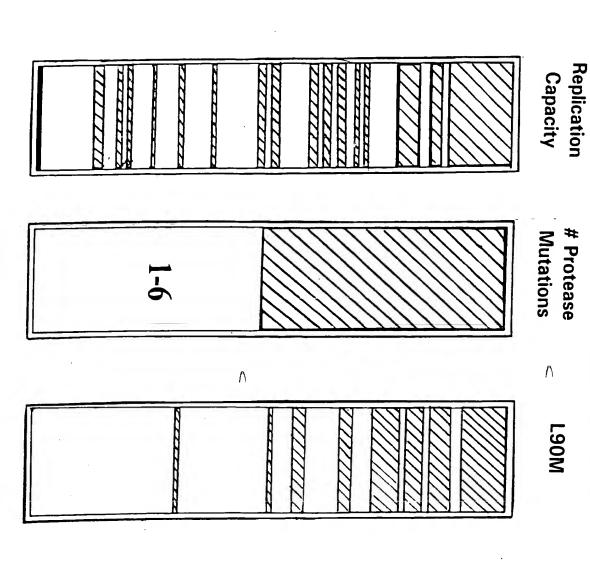


Figure H: Relation of NRTI and NNRTI

Resistance to Replication Capacity

Figure I: Low Replication Capacity is Associated with High Numbers of Mutations in Protease and L90M



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## Figure J: Low Replication Capacity is Associated With Specific Protease Mutations

D30N

L90M PLUS mutations at 73, 20, 46, or 88

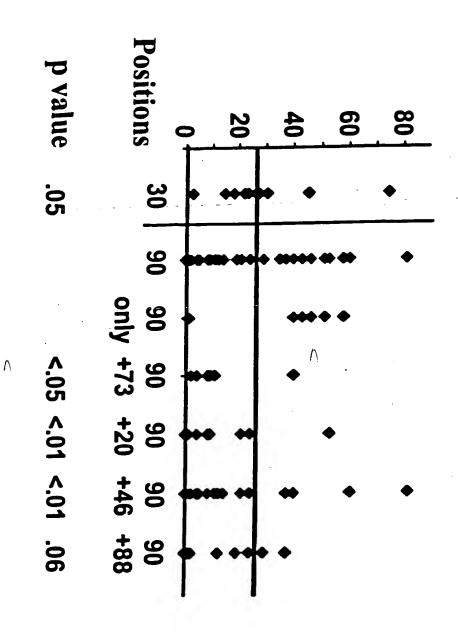
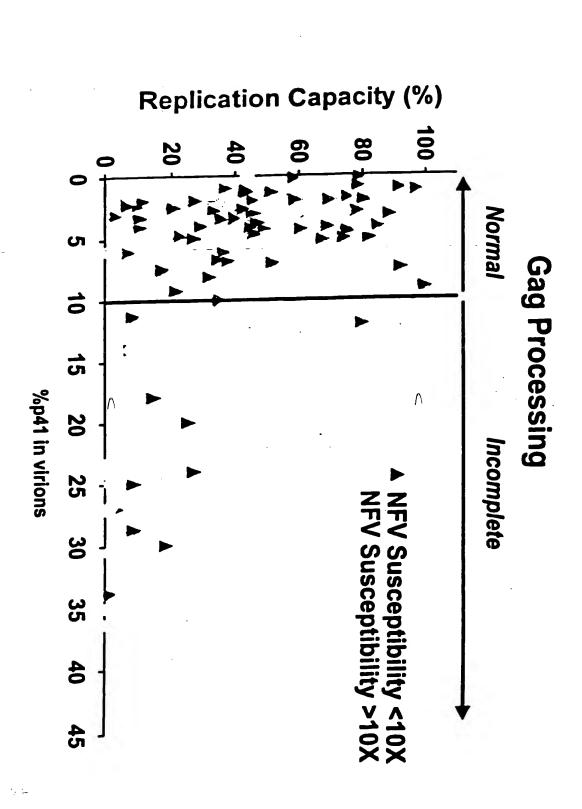
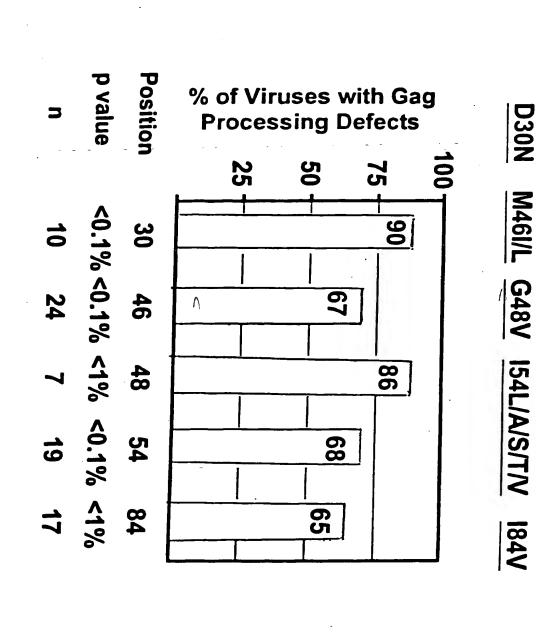


Figure K: Relation of NFV Phenotypic Drug Susceptibility, gag Processing and Replication Fitness



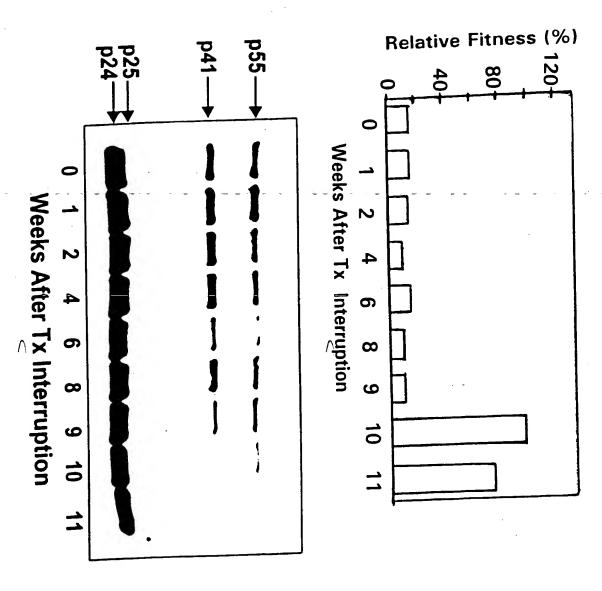
### Figure L: Mutations in PR Associated with Gag **Processing Defects**



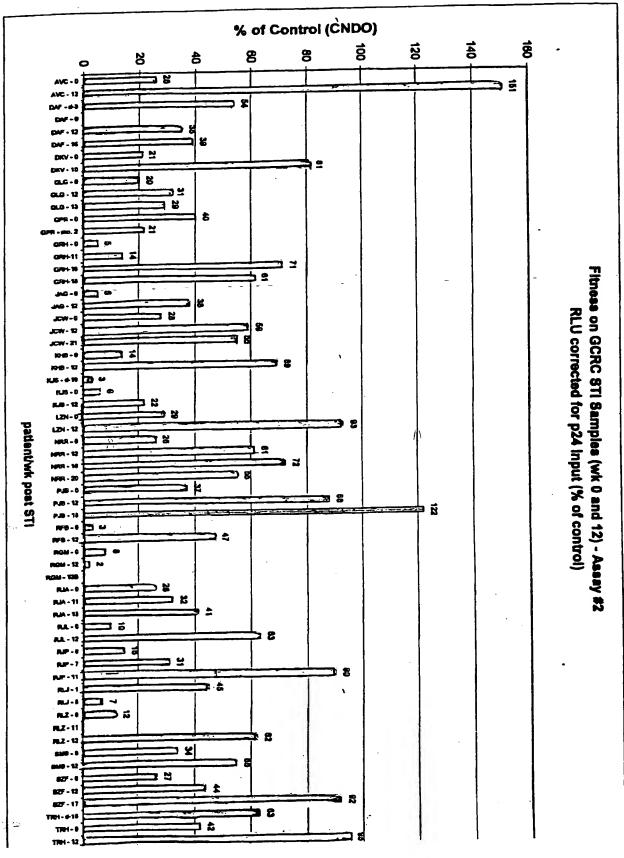
	Σ	വ	1	2	ω	4	ъ	6	7	/22		T 12	Τμ	
	WEEK	day 0					J.	J.	,		10	11	12	23
NRTI	AZT	3.7	4.5	5.8	6.5	6.3	6.4	5.0	9.1	2.8	1.5	0.9	0.8	0.7
	ЗТС	>100	>100	>100	>100	>100	>100	>100	>100	8.1	1.7	1.2	1.3	1.1
	D4T	2.8	3.3	3.2	2.7	3.1	3.0	2.8	4.1	1.9	1.1	1.0	0.8	1.0
	ABC	19	20	14	15	15	17	19	12	5.0	1.3	1.2	1.2	0.6
	NVP	>300	>300	>300	>300	>300	>300	>300	>300	22	1.7	0.8	0.5	0.8
NNRTI	DLV	88	78	75	96	94	76	93	89	15	2.0	1.1	1.0	1.1
	EFV	115	134	142	183	174	119	168	154	10	1.6	0.9	0.8	0.8
	SQV	85	95	89	59	59	59	89	85	1.8	0.9	1.0	0.8	0.8
	IDV	72	74	77	75	89	60	39	78	3.5	1.6	1.1	0.8	0.8
PI	RTV	73	59	49	52	50	54	80	53	4.7	1.9	1.1	0.9	1.0
	NFV	74	80	59	51	49	36	40	53	4.0	1.8	1.1	1.1	0.9
	AMP	16	21	19	15	15	10	18	19	2.0	1.6	1.0	0.8	0.6

Figure M: Patient Virus Reversion to Drug Susceptibility after Treatment Interruption

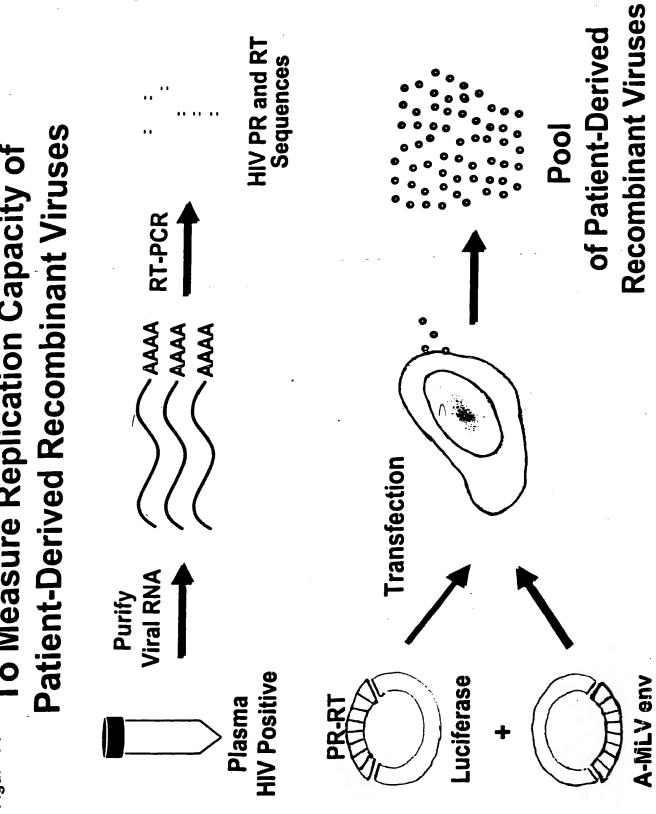
Figure N: Patient Virus Reversion to Normal Replication Fitness after Treatment Interruption



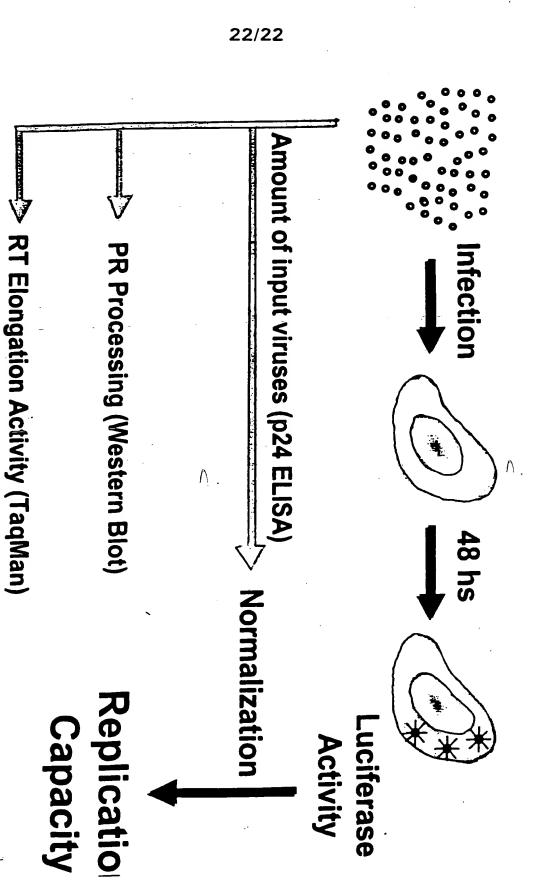
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To Measure Replication Capacity of



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